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Health and Environmental Effects Profile for Methylene Bromide

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR METHYLENE BROMIDE

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16. ABSTRACT

The Health and Environmental Effects Profile for Methylene Bromide was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents. Quantitative estimates have been presented provided sufficient data are available. Methylene bromide has been determined to be a systemic toxicant. A Reference Dose (RfD), defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effect during a lifetime, for methylene bromide is 0.01 mg/kg/day for inhalation exposure. The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. The RQ value for methylene bromide is 1000.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1985.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic exposures. An RfD is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, RfDs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

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EXECUTIVE SUMMARY

Methylene bromide (dibromomethane) is a clear, colorless liquid (Hawley, 1981) which has limited uses in syntheses, as a solvent and in gage fluids (Stenger, 1978). It is soluble in several organic solvents and is slightly soluble in water (Hawley, 1981). According to the public portion of the U.S. EPA TSCA Production File for 1977, Dow Chemical Co. manufactured between 1 and 10 million pounds of methylene bromide (U.S. EPA, 1977). Dow Chemical and Vineland Chemical currently manufacture this compound in the United States (SRI, 1985). No data regarding recent production volumes of this chemical are available.

If methylene bromide is released to surface water then volatilization is expected to be the dominant fate mechanism for methylene bromide released to environmental surface waters. The volatilization half-life from a river 1 m deep flowing 1 m/sec with a wind velocity of 3 m/sec is estimated to be 5.2 hours by the method of Lyman et al. (1982). Hydrolysis, oxidation, direct photolysis, microbial degradation, adsorption and bioconcentration are not expected to be competitive processes with volatilization in surface waters. If released to the atmosphere, methylene bromide will react with photochemically produced hydroxyl radicals at a theoretically estimated half-life of 1.3 years (U.S. EPA, 1986a). Reaction with hydroxyl radicals is expected to be the main method of degradation in the troposphere (Robbins, 1976). Because of the relatively long tropospheric lifetime, ~6% of the methylene bromide present in the troposphere may eventually reach the stratosphere, where direct photolysis will become the dominant loss mechanism. If released to soil, methylene bromide is expected to be highly mobile and,

therefore, may easily leach into groundwater based on an estimated K_{oc} value in the range of 17-25. Volatilization from soil surfaces may be a significant transport mechanism.

Methylene bromide has been detected in drinking water (Coleman et al., 1976; Shackelford and Keith, 1976; Fielding et al., 1981; Koch and Tunger, 1981), in surface (concentrations ranged from trace to 358.6 ppb) and groundwaters (concentrations ranged from trace to 44.9 ppb) (Page, 1981; Kaiser et al., 1983), in industrial wastewater effluents (Perry et al., 1979; Wilson, 1981; Shackelford and Keith, 1976) and in seawater (Wakeham et al., 1983). The presence of methylene bromide in seawater may be due to natural formation and release from macroalgae (Gschwend et al., 1985). Water chlorination treatment may inadvertently introduce bromo-organic compounds such as methylene bromide (Gould et al., 1983) in potable waters. Atmospheric monitoring studies have detected methylene bromide in source-dominated areas in the United States at a mean concentration of 2.3 ppb (Brodzinsky and Singh, 1982), in the ambient air of Barrows, AK, at an average concentration of 5 ppt, and in the general Arctic atmosphere and haze at 3-60 ppt (Rasmussen and Khalil, 1984; Berg et al., 1984). Volatilization from seawater sources may be a major source of methylene bromide in the global atmosphere (Gschwend et al., 1985).

Data concerning acute toxicity of methylene bromide to aquatic organisms could not be located in the available literature. A study with several species of marine algae indicated that these algae can synthesize and release methylene bromide at rates up to 2 ng/g dry wt./day (Gschwend et al., 1985).

Methylene bromide appears to be absorbed after oral and inhalation exposures in rats and rabbits (Dow, n.d.) and dermal exposure in rats and rabbits (Rodkey and Colloson, 1977; McDougal et al., 1985). Methylene bromide was metabolized in vitro to carbon monoxide and inorganic bromide by the microsomal enzymes of the liver, lungs and kidneys, but not of the brain or spleen (Kubic and Anders, 1975). The oxidation appears to be catalyzed by a cytochrome P-450 dependent system (Kubic and Anders, 1975, 1978; Stevens et al., 1980). During dermal exposure, the metabolism of methylene bromide was saturable as indicated by the nonlinear increase in plasma bromide ion concentration (McDougal et al., 1985). Intraperitoneal administration of 522 mg/kg of methylene bromide to male rats resulted in a peak carboxyhemoglobin level of 14% of the hemoglobin concentration at 4 hours of treatment (Kubic et al., 1974). By 10 hours after treatment, the carboxyhemoglobin level was approaching the pretreatment level. Repeated daily exposure did not result in accumulation of carboxyhemoglobin. Methylene bromide may also undergo metabolism by glutathione conjugation (Van Bladeren et al., 1980, 1981). The only information regarding the excretion of methylene bromide is that the metabolite, carbon dioxide, is excreted in the exhaled air (Rodkey and Collison, 1977).

Although methylene bromide is mutagenic to some strains of S. typhimurium (TA100 and TA1950) and E. coli (WU 361089 and K39) without metabolic activation, the carcinogenicity of methylene bromide has not been adequately evaluated. Pertinent data regarding the teratogenic or reproductive effects of methylene bromide could not be located in the available literature as cited in the Appendix. No effects were observed in rabbits treated orally with 60 doses of 300 mg/kg for 92 days, but 400 mg/kg produced marked anesthesia (Dow, n.d.). Rats exposed by inhalation to 900-1000 ppm (6400-7111

mg/m³), 7 hours/day for up to 54 exposures had increased mortality, signs of CNS toxicity and histological changes in lungs, liver and kidneys. Rats and rabbits exposed to 200 ppm (1422 mg/m³) 79 times in 114 days had liver and kidney lesions. No gross or histological effects were observed in rats or dogs exposed to 150 ppm (1067 mg/m³) for 6 hours/day, 60-70 times in 90 days (Dow, n.d.; Keyes et al., 1982). Female rats exposed to 75 or 1500 ppm (533 or 1067 mg/m³) had a slight increase in liver weight (Keyes et al., 1982). Both sexes of rats had dose-related increases in percent carboxyhemoglobin saturation of the blood at $\geq$25 ppm ($\geq$178 mg/m³), but the increase at 25 ppm was not biologically significant. Dogs had significantly increased carboxyhemoglobin saturation only at 150 ppm. Rats exposed for 90 days and observed up to 2 years had decreased body weight gain at 75 and 150 ppm.

Based on the inhalation NOAEL of 25 ppm (178 mg/m³), 6 hours/day, 63 times in 90 days, in the Keyes et al. (1982) study, an RfD of 0.01 mg/kg/day or 0.8 mg/day for a 70 kg human was derived. An RQ of 1000 was derived based on increased liver and kidney lesions in mice exposed by inhalation in the Dow (n.d.) study. Data regarding the carcinogenicity of methylene bromide were inadequate; therefore, it is classified as a U.S. EPA (1986c) class D chemical.

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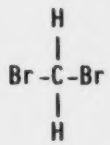
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
CAS	Chemical Abstract Service
CNS	Central nervous system
CS	Composite score
K_{oc}	Soil sorption coefficient standardized with respect to organic carbon
K_{ow}	Octanol/water partition coefficient
LD_{50}	Dose lethal to 50% of recipients
LOAEL	Lowest-observed-adverse-effect level
MED	Minimum effective dose
NADPH	Nicotinamide adenine dinucleotide phosphate (reduced form)
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
ppb	Parts per billion
ppm	Parts per million
ppt	Parts per trillion
Rfd	Reference dose
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value
TLV	Threshold limit value
TWA	Time-weighted average

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Methylene bromide is the common chemical name, but this compound is also known as dibromomethane and methylene dibromide. The structure, molecular weight, empirical formula and CAS Registry number for methylene bromide are as follows:



Molecular weight: 173.86

Empirical formula: CH_2Br_2

CAS Registry number: 74-95-3

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Methylene bromide is a clear, colorless liquid that is miscible with alcohol, ether, chloroform or acetone (Hawley, 1981). Selected physical properties of methylene bromide are listed below:

Melting point:	-52.7°C	Stenger, 1978
Boiling point:	96.9°C	Stenger, 1978
Density (20/4°C):	2.497 g/cm³	Stenger, 1978
Refractive index (20°C):	1.542	Stenger, 1978
Vapor pressure (mm Hg):		
at 0°C	11.5	Kudchadker et al., 1979
at 9.7°C	20.0	Perry and Green, 1984
at 15.0°C	26.7	Kudchadker et al., 1979
at 20.0°C	34.6	Kudchadker et al., 1979
at 25.0°C	44.2	Kudchadker et al., 1979
Water solubility:		
at 15°C	11.70 g/1000 g	Gross and Saylor, 1931
at 25°C	11.5 g/ℓ	Hine and Mookerjee, 1975
at 30°C	11.93 g/1000 g	Gross and Saylor, 1931
Log K_{ow}:	1.529 (calculated)	U.S. EPA, 1986a

Methylene bromide is nonflammable (Hawley, 1981). It is chemically stable and does not undergo hydrolysis and photolysis under ordinary conditions (Chapter 2).

1.3. PRODUCTION DATA

According to the public portion of the U.S. EPA TSCA Production File, Dow Chemical Co., Midland, MI, manufactured between 1 and 10 million pounds and Velsicol Chemical Corp., St. Louis, MI, manufactured an undisclosed amount of methylene bromide in 1977 (U.S. EPA, 1977). Methylene bromide is currently manufactured in the United States by Dow Chemical, Midland, MI, and by Vineland Chemical, Vineland, NJ (SRI, 1985). Data regarding recent production volumes are not available.

Methylene bromide is manufactured by reacting methylene chloride with either hydrogen bromide or aluminum bromide in the presence of catalysts, followed by washing with water and distillation (Stenger, 1978).

1.4. USE DATA

Methylene bromide has limited uses in syntheses, as a solvent and in gage fluids. It has potential uses as a dense, volatile media for mineral and salts gravity separations (Stenger, 1978).

1.5. SUMMARY

Methylene bromide (dibromomethane) is a clear, colorless liquid (Hawley, 1981) which has limited uses in syntheses, as a solvent and in gage fluids (Stenger, 1978). It is soluble in several organic solvents and is slightly soluble in water (Hawley, 1981). According to the public portion of the U.S. EPA TSCA Production File for 1977, Dow Chemical Co. manufactured between 1 and 10 million pounds of methylene bromide (U.S. EPA, 1977). Dow Chemical and Vineland Chemical currently manufacture this compound in the United States (SRI, 1985). No data regarding recent production volumes of this chemical are available.

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. WATER

2.1.1. Hydrolysis. The hydrolysis half-life of methylene bromide in water at 25°C and pH 7 has been estimated to be 183 years (Mabey and Mill, 1978), indicating that hydrolysis is not expected to be environmentally relevant.

2.1.2. Oxidation. The oxidation of methylene bromide in natural water by peroxy radicals or singlet oxygen is not expected to be significant, based on reaction rates estimated for methyl bromide and tribromomethane (Mabey et al., 1981).

2.1.3. Photolysis. Methyl bromide and tribromomethane do not significantly absorb light of wavelengths >290 nm, and direct photolysis of these compounds, which are similar in structure to methylene bromide, is not expected to be environmentally significant (Robbins, 1976; Mabey et al., 1981). Therefore, methylene bromide is not expected to directly photolyze in the environment. Ollis (1985) has shown that titanium dioxide (0.1 wt. %) catalyzes the photolysis of methylene bromide in water at environmentally significant wavelengths.

2.1.4. Microbial Degradation. Pertinent data regarding the biodegradation of methylene bromide could not be located in the available literature as cited in the Appendix. Callahan et al. (1979) estimated that biodegradation is probably not a significant fate mechanism for methyl bromide, but higher halogen substituted methanes may be metabolized by seaweeds, molluscs, sponges and bacteria present in natural water.

2.1.5. Volatilization. Based on experimental gas phase/aqueous solution equilibrium data (Hine and Mookerjee, 1975), the Henry's Law constant for methylene bromide at 25°C is 8.7×10^{-4} atm-m³/mol. This value of Henry's

Law constant indicates that volatilization of methylene bromide from water to the atmosphere is relatively rapid and significant in the environment, particularly in shallow waters (Lyman et al., 1982). Given this Henry's Law constant and the method of Lyman et al. (1982), the volatilization half-life from a river 1 m deep flowing 1 m/sec with a wind velocity of 3 m/sec can be estimated to be 5.2 hours. This estimation does not take into account any possible effect of sorption on volatilization.

2.1.6. Adsorption. Experimental absorption data could not be located in the available literature; however, the relatively high water solubility (11,500 ppm at 25°C) and low log K_{ow} value (1.5) of methylene bromide suggest that partitioning from the water column to particulate organic matter and sediment in water will not be important.

2.1.7. Bioconcentration. In the absence of experimental data, the BCF value of this chemical has been estimated from the following regression equations for an organic chemical (Lyman et al., 1982):

$$\log BCF = 0.76 \log K_{ow} - 0.23 \qquad (2\text{-}1)$$

$$\log BCF = 2.791 - 0.564 \log WS \text{ (in ppm)} \qquad (2\text{-}2)$$

For methylene bromide, the BCF values calculated from Equations 2-1 and 2-2 are 8.6 and 3.2, respectively, based on a log K_{ow} of 1.529 and a water solubility of 11,500 ppm. The BCF values indicate that methylene bromide is not expected to bioconcentrate significantly in aquatic organisms.

2.2. AIR

2.2.1. Reaction with Hydroxyl Radical. Experimental rate data could not be located in the available literature. Using the U.S. EPA Fate of Atmospheric Pollutants data base system, the rate constant for the gas-phase reaction of methylene bromide and photochemically produced hydroxyl radicals in the atmosphere was estimated to be 2.139×10^{-14} cm^3/molecule-sec at

25°C, which corresponds to a half-life of 1.3 years at an atmospheric hydroxyl radical concentration of $8x10^5$ molecules/cm^3 (U.S. EPA, 1986a).

In the troposphere, the main method of methyl bromide degradation is reaction with hydroxyl radicals (Robbins, 1976), which has a half-life of ~1 year. This is likely to be the case for methylene bromide as well. Given a troposphere to stratosphere turnover lifetime of 30 years and based on a tropospheric lifetime of 1.88 years, ~6% of the methylene bromide present in the troposphere may eventually reach the stratosphere. Upon reaching the stratosphere, the methylene bromide may be expected to undergo direct photolysis to produce bromine, which may react with the stratospheric ozone layer, causing the depletion of ozone similar to that which occurs with methyl bromide.

2.2.2. Photolysis. Methylene bromide is not expected to undergo significant direct photolysis in the environment (see Section 2.1.3.).

2.2.3. Physical Removal Processes. Physical removal of methylene bromide from the atmosphere is not expected to be significant because methylene bromide, which undergoes dissolution into clouds or experiences wash-out, is likely to revolatilize into the air.

2.3. SOIL

2.3.1. Chemical and Microbial Degradation. Pertinent chemical and microbial degradation data for methylene bromide in soil could not be located in the available literature as cited in the Appendix.

2.3.2. Leaching/Adsorption. Experimental data could not be located in the available literature. Estimating the K_{oc} from the water solubility (11,500 ppm) and the regression equation of Kenaga (1980) yields a K_{oc} value of ~25. Estimating the K_{oc} from the molecular topology and quantitative structure-activity relationship analysis method of Sabljic (1984)

yields a K_{oc} value of ~17. These K_{oc} values indicate high soil mobility; therefore, leaching may be expected in most soil types.

2.3.3. Volatilization. The high vapor pressure of methylene bromide (44.2 mm Hg at 25°C) suggests rapid evaporation from dry surfaces. In addition, volatilization from wet soil is also expected to be relatively rapid since the compound volatilizes significantly from water surfaces (see Section 2.1.5.). Therefore, volatilization from soil surfaces may be a significant transport mechanism.

2.4. SUMMARY

Volatilization is expected to be the dominant fate mechanism for methylene bromide released to environmental surface waters. The volatilization half-life from a river 1 m deep flowing 1 m/sec with a wind velocity of 3 m/sec is estimated to be 5.2 hours by the method of Lyman et al. (1982). Hydrolysis, oxidation, direct photolysis, microbial degradation, adsorption and bioconcentration are not expected to be competitive processes with volatilization in surface waters. If released to the atmosphere, methylene bromide will react with photochemically produced hydroxyl radicals at a theoretically estimated half-life of 1.3 years (U.S. EPA, 1986a). Reaction with hydroxyl radicals is expected to be the main method of degradation in the troposphere (Robbins, 1976). Because of the relatively long tropospheric lifetime, ~6% of the methylene bromide present in the troposphere may eventually reach the stratosphere, where direct photolysis will become the dominant loss mechanism. If released to soil, methylene bromide is expected to be highly mobile and, therefore, may easily leach into groundwater based on an estimated K_{oc} value in the range of 17-25. Volatilization from soil surfaces may be a significant transport mechanism.

3. EXPOSURE

3.1. WATER

Methylene bromide has been qualitatively detected in an unidentified finished drinking water in the United States (Shackelford and Keith, 1976; Kool et al., 1982), in various surface and groundwater sources in the United Kingdom used for drinking water (Fielding et al., 1981; Fawell and Fielding, 1985), and in surface and drinking water in East Germany (Koch and Tunger, 1981). In the U.S. EPA's National Organics Reconnaissance Survey of five cities (Miami, FL, Seattle, WA, Ottumwa, IO, Philadelphia, PA and Cincinnati, OH), methylene bromide was 1 of 72 organic compounds qualitatively detected in the drinking water(s); however, the cities in which methylene bromide was detected and the level of methylene bromide in this water were not specified.

Methylene bromide was detected in 45/377 groundwater samples (concentrations ranged from trace to 44.9 ppb) and in 79/282 surface water samples (concentrations ranged from trace to 358.6 ppb) collected throughout New Jersey from both potable and nonpotable sources (Page, 1981). Kaiser et al. (1983) detected methylene bromide at 9/17 sampling locations on the lower Niagara River (concentrations of trace to 0.005 ppb) and at 55/83 sampling locations on Lake Ontario (concentrations of trace to 0.007 ppb). Methylene bromide has also been qualitatively identified in Narragansett Bay, RI (Wakeham et al., 1983) and in Lake Ontario (Great Lakes Water Quality Board, 1983).

Perry et al. (1979) reported the detection of methylene bromide at a concentration of >100 ppb in 1/63 industrial wastewater effluents collected throughout the United States. Wilson (1981) found levels of 19-61 ppb

methylene bromide in a composite sample of various chemical industry wastewaters. Shackelford and Keith (1976) reported detection of methylene bromide in an unidentified chemical plant effluent.

Methylene bromide can be released to environmental waters by wastewater effluents resulting from its industrial production and use. Gould et al. (1983) suggested that compounds such as methyl bromide can be inadvertently formed during commercial chlorination processes; bromine, which is widely distributed in nature, is oxidized by hypochlorous acid to hypobromous acid, which is capable of forming bromo-organic compounds. It may be possible, therefore, that methylene bromide could be inadvertently formed during certain commercial chlorination operations.

Gschwend et al. (1985) found that methylene bromide appears to be a natural product of the marine environment. A brown macroalgae, Ascophyllum nodosum, not only contains methylene bromide, but consistently releases it to seawater at a mean rate of 680 ng/g algae (dry wt)/day. In addition, a variety of algal species were found to release methyl bromide, tribromomethane, dibromochloromethane, various other alkyl bromides and iodides, and methylene bromide. Based on the estimated global algal biomass and the experimentally determined release rates and assuming that 100% of the compounds released to seawater volatilize, Gschwend et al. (1985) suggested that macroalgae are a major source of volatile organobromine released to the atmosphere.

The gross analysis of data for methylene bromide available from the U.S. EPA STORET database cites 200 observation stations with a maximum concentration of 1.0 ppb and mean and minimum concentrations of 0.99 and 0.5 ppb, respectively (U.S. EPA, 1986b).

3.2. FOOD

Pertinent data regarding the monitoring or presence of methylene bromide in food could not be located in the available literature as cited in the Appendix.

3.3. INHALATION

Methylene bromide has been detected in the ambient atmosphere of various source-dominated areas (areas of commercial production or use) in the United States at a mean concentration of 2.3 ppb (Brodzinsky and Singh, 1982).

Rasmussen and Khalil (1984) monitored the ambient air of Barrow, AK, throughout 1983 and found an average methylene bromide concentration of ~5 ppt; similar average concentrations were detected in the arctic haze. Berg et al. (1984) detected methylene bromide levels of 3-60 ppt in the arctic atmosphere during March and April, 1983.

Sources of methylene bromide emissions to the ambient atmosphere include emissions from its commercial production and use, as suggested by its detection in source-dominated areas and volatilization from seawater sources (see Section 3.1.). Singh et al. (1983) suggested that seawater sources are the dominant source of atmospheric methyl bromide.

Assuming an average atmospheric methylene bromide concentration of >5 ppt (1 ppm = 7.23 ng/m^3) in nonsource-dominated areas and a daily inhalation of 20 m^3 of air, an average daily intake of >140 ng is calculated.

3.4. DERMAL

Only one publication pertinent to dermal monitoring and exposure data was located in the available literature as cited in the Appendix. McDougal et al. (1985) used a specially constructed body exposure chamber to analyze the pharmacokinetics of percutaneous absorption of methylene bromide in rats. The rats were fitted with face masks and received charcoal-filtered

fresh air through positive pressure. Exposures to 500-1000 ppm methylene bromide lasted 4 hours during which time five blood samples were drawn from jugular cannulae for analysis of the compound by gas chromatography. The dermal flux (0.004-0.078 mg/cm²/hour) for each concentration was calculated by dividing the amount absorbed by exposed surface area and duration of exposure. This study showed that a whole-body dermal vapor exposure of methylene brmide is possible and quantitation of penetration can be accomplished using calculations based on achieved blood concentrations and some measure of metabolism.

3.5. SUMMARY

Methylene bromide has been detected in drinking water (Coleman et al., 1976; Shackelford and Keith, 1976; Fielding et al., 1981; Koch and Tunger, 1981), in surface and groundwaters (Page, 1981; Kaiser et al., 1983), in industrial wastewater effluents (Perry et al., 1979; Wilson, 1981; Shackelford and Keith, 1976) and in seawater (Wakeham et al., 1983). The presence of methylene bromide in seawater may be due to natural formation and release from macroalgae (Gschwend et al., 1985). Water chlorination treatment may inadvertently introduce bromo-organic compounds such as methylene bromide (Gould et al., 1983) in potable waters. Atmospheric monitoring studies have detected methylene bromide in source-dominated areas in the United States at a mean concentration of 2.3 ppb (Brodzinsky and Singh, 1982), in the ambient air of Barrows, AK, at an average concentration of 5 ppt, and in the general Arctic atmosphere and haze at 3-60 ppt (Rasmussen and Khalil, 1984; Berg et al., 1984). Volatilization from seawater sources may be a major source of methylene bromide in the global atmosphere (Gschwend et al., 1985).

4. PHARMACOKINETICS

4.1. ABSORPTION

Although quantitative data regarding the gastrointestinal absorption of methylene bromide could not be located in the available literature as cited in the Appendix, the systemic toxicity observed following oral exposure (Section 5.5.) indicates that methylene bromide is absorbed by this route.

Rats exposed by inhalation to 100 μmol/kg (17.4 mg/kg) methylene bromide in a closed rebreathing system exhaled ~70 μmol/kg (~2 mg/kg) of carbon monoxide above endogenous levels for 6 hours (Rodkey and Collison, 1977). Although these data indicate that methylene bromide was absorbed by the pulmonary route, some of the carbon monoxide production may have occurred in the lungs, as lung microsomes are capable of metabolizing methylene bromide to carbon monoxide in vitro (Section 4.3.). Furthermore, McDougal et al. (1985) demonstrated that dermal absorption is substantial.

McDougal et al. (1985) studied the dermal absorption of methylene bromide in male Fischer-344 rats in chambers that provided the rats with fresh air while their bodies were exposed to concentrations of methylene bromide ranging from 500-10,000 ppm (3555-71,108 mg/m^3). A jugular catheter provided the means for obtaining serial blood samples in which plasma levels of methylene bromide and bromide were measured. Methylene bromide was detected in the blood within 20 minutes of the start of exposure at all levels and the plasma levels were concentration-related. Although a steady-state of methylene bromide concentration in the plasma was achieved only at the 500 ppm level after 1/2 hour of exposure, the plasma concentrations began to level off after 1/2 hour of exposure to 1000, 5000 and 10,000 ppm.

4.2. DISTRIBUTION

Pertinent data regarding the distribution of methylene bromide could not be located in the available literature as cited in the Appendix.

4.3. METABOLISM

Methylene bromide was metabolized to carbon monoxide and inorganic bromide *in vitro* in the presence of rat hepatic microsomes, NADPH and molecular oxygen (Kubic and Anders, 1975, 1978). Microsomes from rat pulmonary and renal microsomes showed ~18 and ~5%, respectively, of the activity of the hepatic microsomes. Brain and splenic microsomes did not metabolize methylene bromide to carbon monoxide and inorganic bromide. *In vitro* studies with inhibitors and stimulators of cytochrome P-450 activity indicate that a cytochrome P-450 system is involved in the metabolism (Kubic and Anders, 1975; Stevens et al., 1980).

Administration of methylene bromide to rats *in vivo* resulted in increased levels of carboxyhemoglobin, indicative of metabolism of methylene bromide to carbon monoxide and inorganic bromide (Kubic et al., 1974). Kubic et al. (1974) administered 3.0 mmol/kg (522 mg/kg) methylene bromide by intraperitoneal injection to young adult male Long-Evans rats and measured the increase in blood carboxyhemoglobin levels for 10 hours. At 4-5 hours, the carboxyhemoglobin level peaked at ~14% of the total hemoglobin content of methylene bromide-treated rats. The level then declined in a biphasic manner over the next 5-6 hours.

When the rats were injected intraperitoneally with 3 mmol/kg methylene bromide once daily for 4 days, no evidence of accumulation of carboxyhemoglobin was found.

In the dermal exposure experiments by McDougal et al. (1985) (see Section 4.1.), the bromide ion concentration in plasma increased with increasing exposure concentration in a nonlinear manner, indicating that the metabolism of methylene bromide to inorganic bromide may become saturated at high exposure concentrations.

Rodkey and Collison (1977) reported that the rate of carbon monoxide exhalation by female rats exposed by inhalation to 100 μmol/kg of methylene bromide for up to 6 hours was increased 51 times above the rate of carbon monoxide exhalation by untreated rats.

Van Bladeren et al. (1980, 1981) proposed that, like 1,2-dibromoethane, methylene bromide also undergoes conjugation with glutathione because metabolic activation with liver cytosol, which contains glutathione S-transferase, increased the mutagenicity of methylene bromide to Salmonella typhimurium.

4.4. EXCRETION

Although the amount of carbon monoxide exhaled increased after inhalation exposure of female rats to methylene bromide (Rodkey and Collison, 1977) (see Section 4.3.), pertinent data regarding the percent of an oral or inhalation dose excreted from the body in feces, urine, bile, expired air or sweat could not be located in the available literature as cited in the Appendix.

4.5. SUMMARY

Methylene bromide appears to be absorbed after oral and inhalation exposure in rats and rabbits (Dow, n.d.) and dermal exposure in rats and rabbits (Rodkey and Colloson, 1977; McDougal et al., 1985). Methylene bromide was metabolized in vitro to carbon monoxide and inorganic bromide by the microsomal enzymes of the liver, lungs and kidneys, but not of the brain

or spleen (Kubic and Anders, 1975). The oxidation appears to be catalyzed by a cytochrome P-450 dependent system (Kubic and Anders, 1975, 1978; Stevens et al., 1980). During dermal exposure, the metabolism of methylene bromide was saturable as indicated by the nonlinear increase in plasma bromide ion concentration (McDougal et al., 1985). Intraperitoneal administration of 522 mg/kg methylene bromide to male rats resulted in a peak carboxyhemoglobin level of 14% of the hemoglobin concentration at 4 hours of treatment (Kubic et al., 1974). By 10 hours after treatment, the carboxyhemoglobin level was approaching the pretreatment level. Repeated daily exposure did not result in accumulation of carboxyhemoglobin. Methylene bromide may also undergo metabolism by glutathione conjugation (Van Bladeren et al., 1980, 1981). The only information regarding the excretion of methylene bromide is that the metabolite, carbon dioxide, is excreted in the exhaled air (Rodkey and Collison, 1977).

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of orally administered methylene bromide could not be located in the available literature as cited in the Appendix. A group of 100 male rats were observed for 2 years following the termination of a 90-day inhalation exposure (Section 5.5.) to evaluate the oncogenic potential of methylene bromide (Keyes et al., 1982). The rats were exposed to 0, 25, 75 or 150 ppm (178, 533 or 1067 mg/m^3) of methylene bromide for 6 hours/day, 5 days/week for a total of 62 exposures. There was no effect on mortality. After the 2-year observation period, no increased incidences of grossly observed nontumorous or tumor-like lesions were observed at any exposure level. Organ and tissues were not examined microscopically. The National Toxicology Program has not selected this chemical for carcinogenicity testing (NTP, 1986).

5.2. MUTAGENICITY

Mutagenicity studies of methylene bromide are summarized in Table 5-1. Although metabolic activation increases the mutagenicity of methylene bromide (Van Bladeren et al., 1980, 1981), methylene bromide was mutagenic to Salmonella typhimurium strain TA100 without metabolic activation (Buijs et al., 1984; Van Bladeren et al., 1980; Simmon et al., 1977; Simmon, 1977, 1981; Osterman-Golkar et al., 1983). Methylene bromide was also mutagenic without metabolic activation to base-pair substitution sensitive S. typhimurium strain TA1950 and to Escherichia coli strains K39 and WU 361189, but not to S. typhimurium strain TA1535 or E. coli strain Sd-4 (Osterman-Golkar et al., 1983). In an unpublished Dow (n.d.) study, methylene bromide with metabolic activation was reported not to cause increased mutagenicity in three unspecified strains of S. typhimurium, but to be weakly mutagenic to Saccharomyces cerevisiae strain D3.

TABLE 5-1

Mutagenicity Testing of Methylene Bromide

Indicator/ Organism	Strain	Application	Concentration or Dose	Activating System	Response	Comment	Reference
Salmonella typhimurium	TA100 TA1530 TA1535	spot test	10 µmol/plate	none	+	The negative results obtained in tester strains TA1530 and TA1535 are probably due to the high toxicity found for methylene bromide in these strains. It is unknown why it was not also highly toxic to TA100.	Buijs et al., 1984
S. typhimurium	TA100	plate incorporation	0-10 mM solutions	+/- S-9 or glutathione-S-transferase	+/+	A dose-related response was observed with increasing concentration of methylene bromide in the absence of metabolic activation. S9 mix or added glutathione-S-transferase enhanced the mutagenic response.	Van Bladeren et al., 1980
S. typhimurium	TA100	plate incorporation	0-10 µL/ desiccator	none	+	Because of its volatility, methylene bromide may not be mutagenic in standard plate incorporation assays.	Simmon et al., 1977; Simmon, 1977, 1981
S. typhimurium Escherichia coli	TA1950 TA100 TA1535 Sd-4 WU 361089 K39 (λ)	spot test in desiccator	10 µL/plate	none	+ + - - + +		Osterman-Golkar et al.,1983
	TA100	liquid suspension test	0-30 mM for 2 hours at 37°C	none	+	A dose-related response was observed although formaldehyde is produced in bacterial suspensions in the presence of methylene bromide, the increased frequency of mutation observed after exposure to methylene bromide is greater than the mutagenic effect of formaldehyde alone	

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5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of methylene bromide could not be located in the available literature as cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding the reproductive effects of methylene bromide could not be located in the available literature as cited in the Appendix.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

The only data available on the subchronic or chronic toxicity of methylene bromide were unpublished Dow Chemical Company studies (Dow, n.d.; Keyes et al., 1982) and a Russian inhalation study (Dykan, 1964). The data for one oral toxicity experiment and two inhalation toxicity experiments by Dow (n.d.) were available only in a review by Torkelson and Rowe (1981). In the oral study, no effects on weight gain, general appearance or liver histology were observed in a small group of rabbits (number and sex not specified) treated orally with 300 mg/kg of methylene bromide for 60/92 days. Marked anesthesia, however, was observed in rabbits (number and sex not specified) treated with 400 mg/kg of methylene bromide for 60/92 days (Dow, n.d.).

In the first inhalation study (Dow, n.d.), 10 male and 10 female rats and 1 male and 1 female rabbit were exposed to 900-1000 ppm (6400-7111 mg/m^3) of methylene bromide for 7 hours. After a total of 30-40 exposures, the rats were uncoordinated with a staggering gait, failed to gain weight, had histopathological changes in the lungs, liver and kidneys and, possibly, showed an increased mortality rate. The rabbits had liver and kidney degeneration after exposure to 900-1000 ppm methylene bromide on 54/73 days. In the second inhalation study (Dow, n.d.), histological alterations were observed in the liver and kidneys of rats and rabbits (sex and number unspecified) exposed to 200 ppm (1422 mg/m^3) methylene bromide

for an unspecified number of hours for 79/114 days. The male rats receiving this treatment also had increased liver weight. In a third inhalation study by Dow (Keyes et al., 1982), groups of 115 male and 15 female Sprague-Dawley rats and groups of three male beagle dogs were exposed to 0, 25, 75 or 150 ppm (0, 178, 533 or 1067 mg/m^3) methylene bromide for 6 hours/day, 5 days/week for a total of 62 (male rats), 63 (female rats) or 70 (dogs) exposures within a 90-day period. After the 90-day exposure period, all dogs, 15 male rats and all the female rats were killed and given complete gross pathological examinations. In addition, comprehensive histological examination of 5 male and 5 female rats and all dogs from each of the control and 150 ppm groups were performed. Dogs in the 25 and 75 ppm groups were also examined microscopically for lesions of lung trachea and thoracic lymph nodes. Of the remaining 100 male rats/group, 10 males/group were observed for 1 year and 90 males/group were observed for 2 years. All rats that died or were killed after 1 or 2 years were given complete necropsies. Comprehensive histological examinations were performed on 6, 2, 1 and 5 rats in the control, 25, 75 and 150 ppm groups, respectively, sacrificed after 1 year. Rats killed after 2 years were not examined histologically. In addition to pathological observations, the following parameters were monitored throughout the study: clinical signs, body weight changes, mortality, organ weights, hematology (90-day and 1-year). Dogs were also given ophthalmoscopic examinations. There were slight increases in liver weight in female rats at 75 or 150 ppm and dose-related increases in percent saturation of carboxyhemoglobin at $\geq$25 ppm in both sexes of rats and at 150 ppm in dogs in the 90-day study. The increased percent carboxyhemoglobin saturation at 25 ppm was considered to be biologically insignificant. Decreased mean body weight gain beginning on day 121 occurred among rats exposed to 75 or 150 ppm for 90 days and observed for up to 2 years.

Dykan (1962) reported that alterations in the hepatic regulation of prothrombin and glycogen were observed in rats (number and sex not specified) exposed by inhalation to 0.25 mg/ℓ (250 mg/m³) methylene bromide 4 hours/day for 60 days. Dystrophic effects in the kidneys and liver were observed in rabbits (number and sex not specified) exposed to 2.5 mg/ℓ (2500 mg/m³) for 10 days (duration of exposure not specified) (Dykan, 1964). As noted by Torkelson and Rowe (1981), these Russian reports are not consistent with the inhalation study using rats and dogs by Dow (n.d.), which was a more extensive study.

5.6. OTHER RELEVANT INFORMATION

The acute oral LD_{50} for rats was reported to be >1000 mg/kg methylene bromide (Dow, n.d.). Methylene bromide was slightly irritating to the skin of rabbits, but systemic effects were not reported (Dow, n.d.).

Although many halogenated methanes (e.g., carbon tetrachloride, chloroform and dichloromethane) inhibit the ability of the pulmonary endothelial cells to absorb 5-hydroxytryptophan from the blood, exposure of the isolated perfused rat lung to up to 6000 ppm of methylene bromide had no effect on the ability of pulmonary endothelial cells to absorb 5-hydroxytryptophan (Hede et al., 1985).

Carboxyhemoglobin levels ranged from 12-23% of total hemoglobin after nonsmokers were exposed to 500 ppm of dichloromethane for 8 hours (Fodor and Roscovanu, 1976). The elevated carboxyhemoglobin level did not return to normal for 24-26 hours. Exposure of groups of rats to 1000 ppm methylene bromide or 1000 ppm dichloromethane for 3 hours indicated that methylene bromide was ~2 times as effective as dichloromethane in elevating blood carboxyhemoglobin levels (Fodor and Roscovanu, 1976). In addition, the

carboxyhemoglobin level continued to rise for 4 hours after cessation of treatment in the methylene bromide-treated rats, but not in the dichloromethane-treated rats.

5.7. SUMMARY

Although methylene bromide is mutagenic to some strains of S. typhimurium (TA100 and TA1950) and E. coli (WU 361089 and K39) without metabolic activation, the carcinogenicity of methylene bromide has not been adequately evaluated. Pertinent data regarding the teratogenic and reproductive effects of methylene bromide could not be located in the available literature as cited in the Appendix. No effects were observed in rabbits treated orally with 60 doses of 300 mg/kg for 92 days, but 400 mg/kg produced marked anesthesia (Dow, n.d.). Rats exposed by inhalation to 900-1000 ppm (6400-7111 mg/m^3), 7 hours/day for up to 54 exposures had increased mortality, signs of CNS toxicity and histological changes in lungs, liver and kidneys. Rats and rabbits exposed to 200 ppm (1422 mg/m^3) 79 times in 114 days had liver and kidney lesions. No gross or histological effects were observed in rats or dogs exposed to 150 ppm (1067 mg/m^3) for 6 hours/day, 60-70 times in 90 days (Dow, n.d.; Keyes et al., 1982). Female rats, however, had slight increases in liver weight at 75 or 150 ppm. Increased percent carboxyhemoglobin saturation at >25 ppm (>178 mg/m^3) in both sexes of rat and at 150 ppm in dogs was observed in the 90-day study (Keyes et al., 1982). The increase at 25 ppm in rats was biologically significant. Decreased body weight gain was observed in male rats exposed to $\geq$75 ppm for 90 days and observed for up to 2 years.

6. AQUATIC TOXICITY

6.1. ACUTE

Pertinent data regarding acute toxicity of methylene bromide to aquatic organisms could not be located in the available literature as cited in the Appendix.

6.2. CHRONIC

Pertinent data regarding chronic toxicity of methylene bromide to aquatic organisms could not be located in the available literature as cited in the Appendix.

6.3. PLANTS

Pertinent data regarding effects of methylene bromide on aquatic plants could not be located in the available literature as cited in the Appendix.

6.4. RESIDUES

Gschwend et al. (1985) reported that eight samples of the marine brown alga, Ascophyllum nodosum, collected near Cape Cod, MA, contained an average of 18 ng/g dry wt. (range ND-98 ng/g) methylene bromide. No methylene bromide was detected in samples of the brown alga, Fucus vesiculosis, the green algae, Enteromorpha linza and Ulva lacta, or the red algae, Gigartina stellata and Chondrus crispus. These authors also measured rates of release of methylene bromide by these species. The following values in ng/g dry wt./day were determined: Ascophyllum nodosum, 680 (range ND-2100); Fucus vesiculosis, 84 (ND-590); Enteromorpha linza, ND-300; Ulva lacta, ND-250; Gigartina stellata, ND; and Chondrus crispus, ND. The fact that algae released much higher amounts than they contained suggests that methylene bromide is rapidly eliminated as soon as it is produced by these algae (Gschwend et al., 1985).

6.5. SUMMARY

Data concerning acute toxicity of methylene bromide to aquatic organisms could not be located in the available literature. A study with several species of marine algae indicated that these algae can synthesize and release methylene bromide at rates up to 2 ng/g dry wt./day (Gschwend et al., 1985).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Pertinent guidelines and standards, including EPA ambient water and air quality criteria, drinking water standards, FAO/WHO ADIs, EPA or FDA tolerances for raw agricultural commodities or foods, and ACGIH, NIOSH or OSHA occupational exposure limits could not be located in the available literature as cited in the Appendix.

Despite the report by Sax (1984) that the ACGIH (1981) recommended a TLV of 20 ppm for methylene bromide, no TLV for this chemical was located in the most recent ACGIH (1985-1986) list of TLVs.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic biota from the effects of methylene bromide could not be located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

The carcinogenicity, teratogenicity, chronic toxicity and reproductive effects of methylene bromide have not been adequately evaluated. Methylene bromide is mutagenic to two strains of S. typhimurium and E. coli in the absence of metabolic activation (Buijs et al., 1984; van Bladeren et al., 1980; Simmon et al., 1977; Simmon, 1977, 1981; Osterman-Golkar et al., 1983); however, the mutagenicity of methylene bromide is increased with metabolic activation (van Bladeren et al., 1980, 1981).

No effects were observed in rabbits treated orally with 60 doses of 300 mg/kg for 92 days, but 400 mg/kg produced marked anesthesia (Dow, n.d.). Rats exposed by inhalation to 900-1000 ppm (6400-7111 mg/m^3), 7 hours/day for up to 54 exposures had increased mortality, signs of CNS toxicity and histological changes in lungs, liver and kidneys. Rats and rabbits exposed to 200 ppm (1422 mg/m^3) for an unspecified number of hours 79 times in 114 days had liver and kidney lesions. No gross or histological effects were observed in rats or dogs exposed to $\leq$150 ppm (1067 mg/m^3), 6 hours/day, 62-70 times in 90 days (Dow, n.d.; Keyes et al., 1982). Female rats exposed to 75 or 150 ppm (533 or 1067 mg/m^3) had a slight increase in liver weight (Keyes et al., 1982). Both sexes of rats had dose-related increases in carboxyhemoglobin saturation of the blood at $\geq$25 ppm ($\geq$178 mg/m^3), but the increase at 25 ppm was not biologically significant. Dogs had significantly increased carboxyhemoglobin saturation only at 150 ppm. Rats exposed for 90 days and observed for up to 2 years had decreased body weight gain at 75 and 150 ppm.

The report of the oral study (Dow, n.d.) was not available during the preparation of this document, but a NOEL was defined for oral exposure and could be used to calculate an RfD (formerly called ADI). For oral exposure, the LOAEL is 261 mg/kg/day (400 mg/kg/day x 60/92 days) and the NOEL is 196 mg/kg/day (300 mg/kg/day x 60/92 days). Dividing 196 mg/kg/day by an uncertainty factor of 1000 (10 for interspecies extrapolation, 10 to approximate chronic exposure and 10 to protect sensitive individuals) yields an RfD of 0.2 mg/kg/day or 14 mg/day for a 70 kg man. Because of the limited detail in which this study was reported and the lack of supporting oral data, this RfD cannot be recommended.

Two of the inhalation studies were not available; therefore, details were not sufficient to adequately assess these studies. In the study reported by Keyes et al. (1982), 25 ppm (178 mg/m^3), 6 hours/day for 63 days in a 90-day period was a NOAEL, since the increase in carboxyhemoglobin saturation was not biologically significant. The 75 ppm (533 mg/m^3) level was the LOAEL (increased carboxyhemoglobin, increased liver weight, decreased body weight gain). The 75 ppm level, 6 hours/day for 70 days in a 90-day period was a NOEL and 150 ppm (1067 mg/m^3) was a LOAEL in dogs. Because small numbers of dogs were used and the exposure of 90 days is substantially less than subchronic for dogs, the NOAEL and LOAEL for rats are more appropriate for risk assessment. The mean body weights were 0.42 kg for male rats and 0.26 kg for female rats, as estimated from growth curves in the study. Using the formula recommended by U.S. EPA (1980), inhalation rates of 0.252 m^3/day for male rats and 0.183 m^3/day for female rats are calculated. Multiplying the exposure levels by 6 hours/24 hours, by 62 days/90 days (male rats) or 63 days/90 days (female rats) by an absorption factor of 0.5 and by the inhalation rates, and dividing by the

body weights results in equivalent oral doses. Thus, the NOAEL of 178 mg/m^3 equals 9.2 mg/kg/day for male rats and 11.0 mg/kg/day for female rats. The LOAEL of 533 mg/m^3 equals 27.5 and 32.8 mg/kg/day for males and females, respectively. Dividing the higher NOAEL of 11 mg/kg/day by an uncertainty factor of 1000 (10 for interspecies extrapolation, 10 for use of a subchronic NOAEL and 10 to protect the most sensitive individuals of the human population) results in an RfD of 0.01 mg/kg/day or 0.8 mg/day for a 70 kg man.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

There are no studies available on the chronic toxicity of methylene bromide. A 90-day inhalation study in rats and dogs was available (Keyes et al., 1982). In addition, despite the inadequacies (unspecified strain, sex, number of animals used, purity and vehicle) oral and inhalation Dow (n.d.) studies summarized by Torkelson and Rowe (1981) can be considered for RQ ranking.

The effects of methylene bromide in rats, rabbits and dogs are summarized in Table 9-1. The effects include increased mortality, liver and kidney lesions, failure to gain weight, an anesthetic response, increased liver weight, decreased body weight gain and increased percent carboxyhemoglobin saturation. Data used to calculate CSs are summarized in Table 9-2. The most severe effect is increased mortality (RV_e=10), which occurred at an equivalent human dose of 153 mg/kg/day. Dividing by 10 because the exposure was subchronic and multiplying by 70 kg results in an MED of 1071 mg/day, which corresponds to an RV_d of 1. Multiplying the RV_d by the RV_e results in a CS of 10, which corresponds to an RQ of 1000.

The anesthetic response (RV_e=7) occurred at an equivalent human dose of 99 mg/kg/day. Dividing this subchronic dose by an uncertainty factor of 10 and multiplying by 70 kg yields an MED of 693 mg/day, which corresponds to an RV_d of 1.2. The RV_d multiplied by the RV_e equals a CS of 8.4, which corresponds to an RQ of 1000.

The lowest equivalent human dose producing liver and kidney lesions (RV_e=6) is 31 mg/kg/day, or 3.1 mg/kg/day when divided by an uncertainty factor of 10 to approximate chronic exposure. Multiplying by 70 kg yields an MED of 217 mg/day, which corresponds to an RV_d of 2.0. Multiplying the RV_d by the RV_e results in a CS of 12, which corresponds to an RQ of 1000.

TABLE 9-1

Toxicity Summary for Methylene Bromide

Route	Species/ Strain	Sex/No. at Start	Average Weight (kg)	Vehicle/ Physical State	Purity	Exposure	Transformed Animal Dose (mg/kg/day)	Equivalent Human Dose[a] (mg/kg/day)	Response	Reference
Oral	rabbit/NR	NR/NR	3.8[b]	NR	NR	400 mg/kg/day for 60/92 days	261	99	anesthetic response	Dow, n.d.
Inhalation	rabbit/NR	M,F/ 1/sex	3.8[b]	air	NR	900-1000 ppm (6400-7111 mg/m³), 7 hours/day for 54/73 days	767[c]	290	liver and kidney degeneration	Dow, n.d.
Inhalation	rabbit/NR	NR/NR	3.8[b]	air	NR	200 ppm (1422 mg/m³), unspecified number of hours but assume 7 hours/day for 79/114 days	151[c]	57	liver and kidney lesions	Dow, n.d.
Inhalation	rat/NR	M,F/ 10/sex	0.35[d]	air	NR	900-1000 ppm (6400-7111 mg/m³) for 7 hours/day for 30-40 exposures (assume 5 days/week)	897[c]	153	failure to gain weight, increased mortality, histo-pathological changes in lung, liver and kidney	Dow, n.d.
Inhalation	rat/NR	NR/NR	0.35[d]	air	NR	200 ppm (1422 mg/m³) assume 7 hours/day for 79/114 days	183[c]	31	liver and kidney lesions	Dow, n.d.
Inhalation	rat/ Sprague-Dawley	F/15	0.26[e]	air	99.6%	75 ppm (533 mg/m³) 6 hours/day, 63 times in 90 days	65.7[f]	10	increased liver weight; increased percent carboxyhemo-globin saturation	Keyes et al., 1982
Inhalation	rat/ Sprague-Dawley	M/115	0.42[e]	air	99.6%	75 ppm (533 mg/m³) 6 hours/day, 62 times in 90 days	55.1[f]	10	increased percent carboxyhemoglobin; decreased body weight gain	Keyes et al., 1982

TABLE 9-1 (cont.)

Route	Species/ Strain	Sex/No. at Start	Average Weight (kg)	Vehicle/ Physical State	Purity	Exposure	Transformed Animal Dose (mg/kg/day)	Equivalent Human Dose[d] (mg/kg/day)	Response	Reference
Inhalation	dog/ beagle	M/3	13.5[e]	air	99.6%	150 ppm (1067 mg/m³) 6 hours/day, 70 times in 90 days	69.2[f]	40	increased percent carboxyhemoglobin saturation	Keyes et al., 1982

[a]Calculated by multiplying the animal transformed dose by the cube root of the ratio of the animal body weight to the human body weight (70 kg)

[b]Reference rabbit body weight (U.S. EPA, 1985)

[c]Calculated by multiplying the concentration by the number of hours/day, number of exposures/duration of study by the animal inhalation rate [0.223 m³/day for rats (U.S. EPA, 1980) and 2.0 m³/day for rabbits (U.S. EPA, 1985)] and dividing by the animal body weight. For the exposure of 6400-7111 mg/m³, the average of 6756 mg/m³ was used. Where inhalation durations were not specified, 7 hours/day was assumed; where number of exposures/duration of study was not specified, 5 days/week was assumed.

[d]Reference rat body weight (U.S. EPA, 1980)

[e]Estimated from growth curves in the study

[f]Calculated by multiplying the concentration by 6 hours/24 hours by the number of exposures/90 days, by the inhalation rates [calculated from body weight according to methods of U.S. EPA (1980) or U.S. EPA (1984) to be 0.183 m³/day for female rats, 0.252 m³/day for male rats and 4.5 m³/day for dogs] and dividing by the body weight.

NR = Not reported

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TABLE 9-2

Composite Scores for Methylene Bromide

Route	Species	Animal Dose (mg/kg/day)	Chronic Human MED* (mg/day)	RV_d	Effect	RV_e	CS	RQ	Reference
Oral	rabbit	261	693	1.2	anesthetic effect	7	8.4	1000	Dow, n.d.
Inhalation	rat	183	217	2	adverse histological changes in liver and kidneys	6	12	1000	Dow, n.d.
Inhalation	rat	897	1071	1	increased mortality	10	10	1000	Dow, n.d.
Inhalation	rat	55.1	70	2.7	decreased body weight gain; increased percent carboxyhemoglobin saturation	4	10.8	1000	Keyes et al., 1982

*The dose was divided by an uncertainty factor of 10 to approximate chronic exposure.

Because failure to gain weight occurred at the same dose that produced increased mortality, a CS for this effect need not be calculated. In the study by Keyes et al. (1982) increased percent carboxyhemoglobin saturation, increased liver weight and decreased body weight gain all occurred at an equivalent human dose of 10 mg/kg/day. These effects warrant an RV_e of 4. Multiplying 10 mg/kg/day by 70 kg and dividing by a UF of 10 to approximate chronic exposure yields an MED of 70 kg/day, which corresponds to an RV_d of 2.7. Multiplying the RV_d by the RV_e yields a composite score (CS) of 10.8, which corresponds to an RQ of 1000.

Examination of Table 9-2 reveals that all CSs correspond to RQs of 1000, but the highest CS was obtained for liver and kidney lesions in rats (Table 9-3).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Pertinent data regarding the carcinogenicity of orally administered methylene bromide could not be located in the available literature as cited in the Appendix. An evaluation of rats for tumors by gross necropsy 2 years following the termination of a 90-day inhalation exposure yielded neagative results (Keyes et al., 1982; see Section 5.1.). Therefore, a potency factor (F) cannot be derived.

According to IARC (1982), methylene bromide cannot be classified as to its carcinogenicity and, therefore, belongs in group 3. According to the U.S. EPA (1986c) classification of chemicals for carcinogenicity, methylene bromide belongs in group D, which consists of chemicals that have not been evaluated adequately.

TABLE 9-3

METHYLENE BROMIDE

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	inhalation
Dose*:	217 mg/day
Effect:	liver and kidney lesions
Reference:	Dow, n.d.
RV_d:	2
RV_e:	6
Composite Score:	12
RQ:	1000

*Equivalent human dose

10. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1981. Documentation of the Threshold Limit Values, 4th ed. Cincinnati, OH. (Cited in Sax, 1984)

ACGIH (American Conference of Governmental Industrial Hygienists). 1985-1986. TLVs: Threshold Limit values for chemical substances and in the work environment with intended changes for 1985-1986. Cincinnati, OH.

Berg, W.W., L.E. Heidt, W. Pollock, P.D. Sperry, R.J. Cicerone and E.S. Gladney. 1984. Brominated organic species in the arctic atmosphere. Geophys. Res. Lett. 11: 429-432.

Brodzinsky, R. and H.B. Singh. 1982. Volatile organic chemicals in the atmosphere: An assessment of available data. Atmospheric Science Center. SRI International, Menlo Park, CA. EPA Contract 68-02-3452. 198 p.

Buijs, W., A. Van der Gen, G.R. Mohn and D.D. Breimer. 1984. The direct mutagenic activity of alpha, omega-dihalogenoalkanes in Salmonella typhimurium. Strong correlation between chemical properties and mutagenic activity. Mutat. Res. 141(1): 11-14.

Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. 1979. Water-related environmental fate of 129 priority pollutants. Volume II. EPA 440/4-79-029b.

Coleman, W.E., R.D. Lingg, R.G. Melton and F.C. Kopfler. 1976. The occurrence of volatile organics in five drinking water supplies using gas chromatography/mass spectrometry. In: Indentif. Anal. Org. Pollut. Water, L.H. Keith, Ed. Ann Arbor Science Publ., Ann Arbor, MI. p. 305-327.

Dow. n.d. Dow Chemical Co., Midland, MI. Unpublished data. (Cited in Torkelson and Rowe, 1981)

Dykan, V.A. 1962. Changes in liver and kidney functions due to methylene bromide and bromoform. Issled. Inst. Gig. Tr. Protzabolevarii. 29: 82-90. (CA 60:8541d)

Dykan, V.A. 1964. Problems on toxicology, clinical practice and work hygiene in the production of bromine-organic compounds. Gig. (Kiev:zdorov'e) Sb. p. 100-103. (CA 63:15429g)

Fawell, J.K. and M. Fielding. 1985. Identification and assessment of hazardous compounds in drinking water. Sci. Total Environ. 47: 317-341.

Fielding, M., T.M. Gibson, H.A. James, K. McLoughlin and C.P. Steel. 1981. Organic micropollutants in drinking water. TR-159. Medmenham, Eng. Water Res. Cent. 49 p.

Fodor, G.G. and A. Roscovanu. 1976. Increased blood-carbon monoxide-content in humans and animals by incorporated halogenated hydrocarbons. Zentralbl. Bakteriol., Parasitenkd., Infektionskr. Hys., Abt. 162(1-2): 34-40.

Gould, J.P., R.E. Ramsey, M. Giabbai and F.G. Pohland. 1983. Formation of volatile haloorganic compounds in the chlorination of municipal landfill leachates. Water Chlorination: Environ. Impact Health Eff. 4: 525-539.

Great Lakes Water Quality Board. 1983. An inventory of chemical substances identified in the Great Lakes Ecosystem. Volume 1 - Summary. Report to the Great Lakes Water Quality Board. Windsor Ontario, Canada. p. 195.

Gross, P.M. and J.H. Saylor. 1931. The solubilities of certain slightly soluble organic compounds in water. J. Am. Chem. Soc. 53: 1744-1751.

Gschwend, P.M., J.K. MacFarlane and K.A. Newman. 1985. Volatile halogenated organic compounds released to seawater from temperate marine macroalgae. Science. 227: 1033-1035.

Hawley, G.G. 1981. The Condensed Chemical Dictionary, 10th ed. Van Nostrand Reinhold Co., New York. p. 677.

Hede, A.R., L. Andersson and C. Post. 1985. Effect of a homologous series of halogenated methanes on pulmonary uptake of 5-hydroxytryptamine in isolated perfused rat lung. Acta. Pharmacol. Toxicol. 57(4): 291-296.

Hine, J. and P.K. Mookerjee. 1975. The intrinsic hydrophilic character of organic compounds. Correlations in terms of structural contributions. J. Org. Chem. 40: 292-298.

IARC (International Agency for Research on Cancer). 1979. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Chemical and Industrial Processes Associated with Cancer in Humans. WHO, IARC, Lyon, France. Vols. 1-20, Suppl. 1, p. 9-11.

IARC (International Agency for Research on Cancer). 1982. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyon, France. Suppl. 4, 13-20, p. 1-29.

Kaiser, K.L.E., M.E. Comba and H. Hunealut. 1983. Volatile halocarbon contaminants in the Niagara River and in Lake Ontario. J. Great Lakes Res. 9(2): 212-223.

Kenaga, E.E. 1980. Predicted bioconcentration factors and soil sorption coefficients of pesticides and other chemicals. Ecotoxicol. Environ. Saf. 4: 26-38.

Keyes, D.G., J.W. Henck, G.C. Jersey, R.J. Kociba, D.J. Schwetz and T.D. Landry. 1982. Methylene bromide: A 90-day repeated inhalation toxicity study in rats and dogs with a subsequent two-year holding period for rats. Toxicology Research Lab., Health and Environmental Sciences, Dow Chemical Co., Midland, MI.

Koch, R. and A. Tunger. 1981. Contamination of water with haloalkanes and -alkenes. Acta. Hydrochim. Hydrobiol. 9(4): 471-475. [CA 95(22):192078n]

Kool, H.J., C.F. Van Kreijl and B.C.J. Zoeteman. 1982. Toxicology assessment of organic compounds in drinking water. Crit. Rev. Environ. Control. 12: 307-357.

Kubic, V.L. and M.W. Anders. 1975. Metabolism of dihalomethanes to carbon monoxide. II. In vitro studies. Drug Metab. Dispos. 3(2): 104-112.

Kubic, V.L. and M.W. Anders. 1978. Metabolism of dihalomethanes to carbon monoxide. III. Studies on the mechanism of the reaction. Biochem. Pharmacol. 27(19): 2349-2355.

Kubic, V.L., M.W. Anders, R.R. Engel, C.H. Barlow and W.S. Caughey. 1974. Metabolism of methylene bromide to carbon monoxide. I. In vivo studies. Drug Metab. Dispos. 2: 53-57.

Kudchadker, A.P., S.A. Kudchadker, R.P. Shukla and P.R. Patnaik. 1979. Vapor pressures and boiling points of selected halomethanes. J. Phys. Chem. Ref. Data. 8: 499-517.

Lyman, W.J., W.F. Reehl and D.H. Rosenblatt. 1982. Handbook of Chemical Property Estimation Methods. McGraw-Hill, NY. p. 15-21 to 15-29, 15-16, 5-4, 5-10.

Mabey, W. and T. Mill. 1978. Critical review of hydrolysis of organic compounds in water under environmental conditions. J. Phys. Chem. Ref. Data. 7: 409.

Mabey, W.R., J.H. Smith, R.T. Podoll, et al. 1981. Aquatic Fate Process Data for Organic Priority Pollutants. U.S. EPA, Monitoring and Data Support Division (WH 553) Office of Water Regulations and Standards, Washington, DC. EPA 440/4-81-014.

McDougal, J.N., G.W. Jepson, H.J. Clewell and M.E Andersen. 1985. Dermal absorption of dihalomethane vapors. Toxicol. Appl. Pharmacol. 79: 150-158.

NTP (National Toxicology Program). 1986. Management Status Report, 3/12/86.

Ollis, D.F. 1985. Contaminant degradation in water heterogeneous photocatalysis degrades halogenated hydrocarbon contaminants. Environ. Sci. Technol. 19: 480-484.

Osterman-Golkar, S., S. Hussain, S. Walles, B. Anderstam and K. Sigvardsson. 1983. Chemical reactivity and mutagenicity of some dihalomethanes. Chem-Biol. Interact. 46(1): 121-130.

Page, G.W. 1981. Comparison of groundwater and surface water for patterns and levels of contamination by toxic substances. Environ. Sci. Technol. 15(12): 1475-1481.

Perry, R.H. and D. Green. 1984. Perry's Chemical Handbook. Physical and Chemical Data, 6th ed. McGraw-Hill, New York.

Perry, D.L., C.C. Chuang, G.A. Jungclaus and J.S. Warner. 1979. Identification of organic compounds in industrial effluent discharges. EPA 600/4-79-016. NTIS PB-294794.

Rasmussen, R.A. and M.A.K. Khalil. 1984. Gaseous bromine in the arctic and arctic haze. Geophys. Res. Lett. 11: 433-436.

Robbins, D.E. 1976. Photodissociation of methyl chloride and methyl bromide in the atmosphere. Geophys. Res. Lett. 3: 213-216.

Rodkey, F.L. and H.A. Collison. 1977. Effect of dihalogenated methanes on the in vivo production of carbon monoxide and methane by rats. Toxicol. Appl. Pharmacol. 40(1): 39-47.

Sabljic, A. 1984. Prediction of the nature and strength of soil sorption of organic pollutants by molecular topology. J. Agric. Food Chem. 32: 243-246.

Sax, N.I. 1984. Dangerous Properties of Industrial Materials, 6th ed. Van Nostrand Reinhold Company, NY. p. 914.

Shackelford, W.M. and L.H. Keith. 1976. Frequency of organic compounds identified in water. U.S. EPA, Athens, GA. EPA-600/4-76-062. 158 p.

Simmon, V.F. 1977. Structural correlations of carcinogenic and mutagenic allyl halides. In: Structural Correlates of Carcinogenesis and Mutagenesis. Proc. Second FDA Office Sci. Summer Symposium. p. 163-171.

Simmon, V.F. 1981. Applications of the Salmonella/microsome assay. In: Short-term Tests Chem. Carcinog. p. 120-126.

Simmon, V.F., K. Kauhanen and R.G. Tardiff. 1977. Mutagenic activity of chemicals identified in drinking water. Dev. Toxicol. Environ. Sci. 2: 249-258.

Singh, H.B., L.J. Salas and R.E. Stiles. 1983. Methyl halides in and over the eastern pacific (40°N-32°S). J. Geophys. Res. 88: 3684-3690.

SRI (Stanford Research Institute). 1985. 1985 Directory of Chemical Producers: United States of America. SRI International, Menlo Park, CA. p. 517.

Stenger, V.A. 1978. Bromine compounds. In: Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed., Vol. 4, M. Grayson and D. Eckroth, Ed. John Wiley and Sons, Inc., New York. p. 253, 252.

Stevens, J.L., J.H. Ratanayake and M.W. Anders. 1980. Metabolism of dihalomethanes to carbon monoxide. 4. Studies in isolated rat hepatocytes. Toxicol. Appl. Pharmacol. 55(3): 484-489.

Torkelson, T.R. and V.K. Rowe. 1981. Halogenated aliphatic hydrocarbons. In: Patty's Industrial Hygiene and Toxicology, Vol. 2B, G. Clayton and F.E. Clayton, Ed. John Wiley and Sons, Inc., New York. p. 3459-3461.

U.S. EPA. 1977. Computer print-out of nonconfidential production data from TSCA inventory. OPTS, CID, U.S. EPA, Washington, DC.

U.S. EPA. 1980. Guidelines and Methodology Used in the Preparation of Health Effects Assessment Chapters of the Consent Decree Water Criteria Documents. Federal Register. 45(231): 49347-49357.

U.S. EPA. 1986a. Graphical Exposure Modeling System (GEMS). Fate of Atmospheric Pollutants (FAP) and Octanol Water Partition Coefficient (CLOGP) data bases. Washington, DC.

U.S. EPA. 1986b. STORET Water Quality Database. Online: April, 1986.

U.S. EPA. 1986c. Guidelines for Carcinogen Risk Assessment. Federal Register. 51(185): 33992-34003.

U.S. EPA. 1986d. Reference Values for Risk Assessment. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste, Washington, DC.

Van Bladeren, P.J., D.D. Breimer, G.M.T. Rotteveel-Smijs and G.R. Mohn. 1980. Mutagenic activation of dibromomethane and diiodomethane by mammalian microsomes and glutathione s-transferases. Mutat. Res. 74: 341-346.

Van Bladeren, P.J., D.D. Breimer, G.R. Mohn and A. Van dergen. 1981. Metabolism and mutagenicity of dibromoethane and dibromomethane. Mutat. Res. 85: 270.

Wakeham, S.G., J.T. Goodwin and A.C. Davis. 1983. Distributions and fate of volatile organic compounds in Narragansett Bay, Rhode Island. Can. J. Fish Aquat. Sci. 40: 304-321.

Wilson, J.L. 1981. Determination of volatile organics in industrial and municipal wastewaters. EPA-460/3-81-07. 81 p.

APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

GLOBAL
TSCATS
CASR online (U.S. EPA Chemical Activities Status Report)
CAS online STN International
TOXLINE
TOXBACK 76
TOXBACK 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP
NTIS
Federal Register

These searches were conducted in April, 1986. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Documentation of the Threshold Limit Values and Biological Exposure Indices, 5th ed. Cincinnati, OH.

ACGIH (American Conference of Governmental Industrial Hygienists). 1985-1986. TLVs: Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1985-1986. Cincinnati, OH. 114 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1983. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., Littleton, MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

Jaber, H.M., W.R. Mabey, S.T. Liu, T.W. Chow and H.L. Johnson. 1984. Data aquisition for environmental transport and fate screening for compounds of interest in the Office of Solid Waste. EPA 600/6-84-010. NTIS PB84-243906. SRI International, Menlo Park, CA.

NTP (National Toxicology Program). 1986. Toxicology Research and Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, N.I. 1979. Dangerous Properties of Industrial Materials, 5th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1984. Directory of Chemical Producers. Menlo Park, CA.

U.S. EPA. 1985. Status Report on Rebuttable Presumption Against Registration (RPAR) or Special Review Process. Registration Standards and the Data Call in Programs. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1985. CSB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (U.S. International Trade Commission). 1985. Synthetic Organic Chemicals. U.S. Production and Sales, 1984, USITC Publ. 1745, Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under Contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Res. Publ. 137, Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California, State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. Prepared for the U.S. EPA, Washington, DC. PB-269605.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data: Book 1: Toxicology Data. Office of Pesticide Programs, U.S. EPA, Washington, DC. EPA 540/9-79-003. NTIS PB 80-196876.